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Androgen dependent mechanisms of pro-angiogenic networks in placental and tumor development

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ABSTRACT

The placenta and tumors share important characteristics, including a requirement to establish effective angiogenesis. In the case of the placenta, optimal angiogenesis is required to sustain the blood flow required to maintain a successful pregnancy, whereas in tumors establishing new blood supplies is considered a key step in supporting metastases. Therefore the development of novel angiogenesis inhibitors has been an area of active research in oncology. A subset of the molecular processes regulating angiogenesis are well understood in the context of both early placentation and tumorigenesis. In this review we focus on the well-established role of androgen regulation of angiogenesis in cancer and relate these mechanisms to placental angiogenesis. The physiological actions of androgens are mediated by the androgen receptor (AR), a ligand dependent transcription factor. Androgens and the AR are essential for normal male embryonic development, puberty and lifelong health. Defects in androgen signalling are associated with a diverse range of clinical disorders in men and women including disorders of sex development (DSD), polycystic ovary syndrome in women and many cancers. We summarize the diverse molecular mechanisms of androgen regulation of angiogenesis and infer the potential significance of these pathways to normal and pathogenic placental function. Finally, we offer potential research applications of androgen-targeting molecules developed to treat cancer as investigative tools to help further delineate the role of androgen signalling in placental function and maternal and offspring health in animal models.

1. Introduction

It has long been recognized that the placenta and tumors share important characteristics. These include mechanisms related to

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